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Supreme Court, U.S.
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No. 02-

IN THE

Supreme Court of the United States

DEE and DON HOLLANDER,

Petitioners,

v.

SANDOZ PHARMACEUTICALS CORPORATION, a New Jersey corporation; SANDOZ LTD., a foreign corporation; and HCA HEALTH SERVICES OF OKLAHOMA, INC., an Oklahoma corporation, d/b/a PRESBYTERIAN HOSPITAL,

Respondents.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE TENTH CIRCUIT

PETITION FOR A WRIT OF CERTIORARI

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QUESTIONS PRESENTED

1. Whether *Caterpillar, Inc. v. Lewis*, 519 U.S. 61 (1996), changed the rule that for diversity jurisdiction purposes the citizenship of a party is determined as of the date of filing suit and the date of removal.

2. Whether the rule in *Koenigsberger v. Richmond Silver Mining Company*, 158 U.S. 41 (1895) and elsewhere, as to the point at which the determination of the citizenship of a party for diversity jurisdiction purposes is made is to be changed in light of *Caterpillar, Inc. v. Lewis*, 519 U.S. 61 (1996).

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CITATION TO OFFICIAL JUDICIAL OPINION

The opinion of the Court of Appeals is reported as *Hollander v. Sandoz Pharmaceuticals Corporation*, 289 F.3d 1193 (10th Cir. 2002), and is reproduced in the Appendix, beginning at p. 1a.

STATEMENT OF BASIS FOR JURISDICTION

On May 10, 2002, the United States Court of Appeals for the Tenth Circuit entered its order affirming a judgment in favor of Respondents. On July 11, 2002, the Tenth Circuit denied the Hollanders' petition for rehearing and request for hearing *en banc*. Review is sought pursuant to 28 U.S.C. § 1254(1) and pursuant to Supreme Court Rule 10(a) and 10(c). The district court's jurisdiction was premised upon 28 U.S.C. § 1441(a) and the jurisdiction of the Tenth Circuit was based upon 28 U.S.C. § 1291.

STATUTORY PROVISION INVOLVED

This petition involves the interpretation and scope of removal jurisdiction under 28 U.S.C. § 1441(a). This provision is set forth in its entirety in the Appendix, beginning at p. 62a.

STATEMENT OF THE CASE

The Hollanders, Petitioners herein, brought suit in the District Court of Oklahoma County, Oklahoma, after Ms. Hollander was paralyzed by ingesting a prescribed drug, Parlodel. A products liability claim was made against the manufacturers and distributors of the drug, who are the Respondents herein.

At the time of filing the lawsuit (and at the time of removal to federal court), the citizenship of all Petitioners was not diverse from the citizenship of all Respondents. Particularly, Petitioner Don Hollander was a citizen of Oklahoma, as was the hospital that dispensed the drug, Respondent HCA Health Services of Oklahoma, Inc.

After the state court judge granted the hospital's motion to dismiss for failure to state a claim, the Respondents Sandoz removed the action to the United States District Court for the Western District of Oklahoma.

Petitioners moved to remand the case to state court on the grounds that the involuntary dismissal of the non-diverse hospital did not confer jurisdiction under controlling Tenth Circuit law. *DeBry v. Transamerica Corp.*, 601 F.2d 480, 486-488 (10th Cir. 1979), following *Whitcomb v. Smithson*, 175 U.S. 635, 20 S. Ct. 248, 44 L. Ed. 303 (1900). Petitioners also pointed out the longstanding rule of this Court that diversity of citizenship is determined as of the time the court jurisdiction is invoked and not later. *Koenigsberger v. Richmond Silver Mining Co.*, 158 U.S. 41, 15 S. Ct. 751, 39 L. Ed. 889 (1895). The district court denied remand.

The dismissal by the state court of the Oklahoma hospital was non-final, interlocutory, and subject to change at any time up to the point of final judgment. 12 O.S. § 994(A); Fed. R. Civ. P. 54(b). The decision as to the hospital became final only when judgment was entered relating to Respondents Sandoz.

Subsequent to removal, Don Hollander moved to Arkansas, where it is assumed he continued to reside at the time the federal district court entered judgment. The result of the action was judgment in favor of all Respondents.

The Tenth Circuit affirmed. On the question of federal court jurisdiction, the Tenth Circuit relied on *Caterpillar, Inc. v. Lewis*, 519 U.S. 61, 17 S. Ct. 467, 136 L. Ed. 2d 437 (1996), which held that where jurisdiction exists at the time of judgment, the lack of jurisdiction in earlier stages of the litigation was not fatal to federal court subject matter jurisdiction. The Tenth Circuit ruled that Don Hollander's move to Arkansas after removal operated to create the diversity of citizenship necessary to sustain the judgment.

REASONS FOR GRANTING THE PETITION

PROPOSITION I:

The Tenth Circuit Opinion Below Conflicts With Relevant Decisions Of This Court.

In a long line of cases, this Court has held that citizenship of parties is determined for diversity jurisdiction purposes as of the time the case is filed and the time the case is removed, and that a change in citizenship subsequent thereto is disregarded. *Koenigsberger v. Richmond Silver Mining Co.*, 158 U.S. 41, 15 S. Ct. 751, 39 L. Ed. 889 (1895); *Gibson v. Bruce*, 108 U.S. 561, 2 S. Ct. 873, 27 L. Ed. 825 (1883); *Stevens v. Nichols*, 130 U.S. 230, 9 S. Ct. 518, 32 L. Ed. 914 (1889); and *Metcalf v. City of Watertown*, 128 U.S. 586, 9 S. Ct. 173, 32 L. Ed. 543 (1888). The Tenth Circuit, by considering that "complete diversity existed between the remaining parties at the time that the federal district court entered judgment" in that the Hollanders resided in Arkansas, ignores the rule in these cases.

The Tenth Circuit ignores the rule in earlier Supreme Court cases because of this Court's 1996 decision in *Caterpillar*. *Caterpillar* held that the failure to remand a case which was improperly removed "is not fatal to the ensuing adjudication if federal jurisdictional requirements are met at the time the judgment is entered." 519 U.S. at 64. However, *Caterpillar* dealt with a situation where the plaintiffs had voluntarily dismissed non-diverse defendants; *Caterpillar* did not address nor explicitly overrule the longstanding principle that the citizenship is determined as of specific points in time and is not affected by subsequent moving of the parties.

Accordingly, *Caterpillar* did not require the maintenance of federal court jurisdiction: at the time judgment was entered in the district court, Don Hollander would have remained, for diversity jurisdiction purposes, a citizen of the State of Oklahoma; the 12(b)(6)-dismissed hospital would also have remained an Oklahoma citizen. Jurisdictional requirements were never met.

The rule in *Caterpillar* is not in conflict with the rule in *Koenigsberger*. Although *Caterpillar* says that the *diversity* of citizenship can be determined at the time of judgment, *Koenigsberger* says when the *citizenship* is determined. The Tenth Circuit erred by not following *Koenigsberger.*

PROPOSITION II:

The Tenth Circuit Decision Is In Conflict With The Decision Of The D.C. Circuit.

The Tenth Circuit ruled that *Caterpillar* allows citizenship to change after removal so as to confer jurisdiction; the United States Court of Appeals for the District of Columbia Circuit has ruled directly contrary on this issue. *Saadeh v. Farouki*, 107 F.3d 52 (D.C. Cir. 1997). In *Saadeh*, the appellee, a foreign national, sought to maintain jurisdiction on the grounds that the appellant became a citizen of the United States during the course of the action. The D.C. Circuit said:

> We conclude, however, that [appellant's] change in citizenship and possible change in domicile could not cure a defect in complete diversity if one existed at the time [appellee] filed his complaint. It is well established that diversity of citizenship is determined at the time the complaint is filed . . . Thus, if parties are diverse at the time of filing, a subsequent change in citizenship or domicile will not divest the court of jurisdiction . . .
>
> [Appellee] cites a number of cases involving removal for the proposition that the court may take account of [appellant's] change in citizenship, but neither these cases nor the Supreme Court's recent decision in *Caterpillar, Inc. v. Lewis*, 117 S. Ct. 467 (1996), support this view. Rather, these cases are consistent with the view that a district court may cure a jurisdictional defect by dismissing a dispensable, non-diverse party pursuant to Rule 21 . . . Although

> we are mindful of the "considerations of finality, efficiency and economy" that concerned the Supreme Court in *Caterpillar*, those concerns in the removal context are insufficient to warrant departure here from the bright-line rule that citizenship and domicile must be determined as of the time a complaint is filed. Indeed, the instant case demonstrates the value of a bright-line rule; even on appeal the parties continue to develop new theories and proffer new evidence on citizenship and domicile.

Accordingly, the decision of the D.C. Circuit is directly in conflict with the decision of the Tenth Circuit.

CONCLUSION

Petitioners request this Court to grant *certiorari* to address and clarify the issue of when citizenship is determined in light of *Caterpillar* and resolve the conflict in the circuits.

Respectfully submitted,

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APPENDIX

APPENDIX A — OPINION OF THE UNITED STATES COURT OF APPEALS FOR THE TENTH CIRCUIT DATED AND FILED MAY 10, 2002

UNITED STATES COURT OF APPEALS

TENTH CIRCUIT

No. 00-6135

DEE HOLLANDER and
DON HOLLANDER,

Plaintiffs - Appellants,

v.

SANDOZ PHARMACEUTICALS CORPORATION, a New Jersey corporation; SANDOZ, LTD., a foreign corporation; and HCA HEALTH SERVICES OF OKLAHOMA, INC., an Oklahoma corporation, d/b/a/ Presbyterian Hospital,

Defendants - Appellees.

APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE WESTERN DISTRICT OF OKLAHOMA (D.C. NO. 96-CV-756-T)

Before **EBEL** and **HENRY**, Circuit Judges, and **ROGERS**, District Judge.*

---

* The Honorable Richard D. Rogers, United States District Judge for the District of Kansas, sitting by designation.

HENRY, Circuit Judge.

Dee and Don Hollander filed this products liability action in the District Court for Oklahoma County alleging that Parlodel, a drug manufactured by Sandoz Pharmaceuticals Corporation ("Sandoz"), now known as Novartis Pharmaceuticals Corporation, and distributed by HCA Health Services of Oklahoma, Inc., doing business as Presbyterian Hospital ("Presbyterian Hospital"), caused Ms. Hollander to suffer an intracerebral hemorrhage shortly after she gave birth to the Hollanders' second child. After the Oklahoma County District Court dismissed the Hollanders' claim against Presbyterian Hospital, the remaining defendants removed the case to the federal district court.

The federal district court denied the Hollanders' motion to remand the case to state court. It rejected the Hollanders' arguments that it lacked jurisdiction over the remaining claims and that the defendants' removal petition was untimely. Subsequently, the federal district court dismissed the defendant Sandoz, Ltd. with prejudice, reasoning that the holding company had its principal place of business in Switzerland and that the court lacked personal jurisdiction over it.

Finally, applying *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), the federal district court ruled that the Hollanders' expert testimony regarding the causal connection between Parlodel and intracerebral hemorrhages lacked the necessary reliability and was therefore inadmissible. *See Hollander v. Sandoz Pharms. Corp.*, 95 F. Supp. 2d 1230, 1238-39 (W.D. Okla. 2000). As a result, the court granted summary judgment to Sandoz.

The Hollanders now appeal those rulings, arguing that: (1) the federal district court lacked subject matter jurisdiction and therefore erred in denying their motion to remand the case to the Oklahoma state court; (2) the court erred in dismissing their claim against the defendant Presbyterian Hospital; (3) the court abused its discretion in ruling that the testimony of their experts was not sufficiently reliable to be admissible; (4) the court erred in granting summary judgment to Sandoz; and (5) the district court erred in dismissing their claim against Sandoz, Ltd., with prejudice.

For the reasons set forth below, we conclude that the federal district court had subject matter jurisdiction. We further hold that the court did not abuse its discretion in finding that the Hollanders' expert testimony was not sufficiently reliable and that the court did not err in granting summary judgment to Sandoz. However, we agree with the Hollanders that the federal district court should have dismissed their claim against Sandoz, Ltd., *without* prejudice. In light of these conclusions, we do not address the Hollanders' challenge to the dismissal of their claim against Presbyterian Hospital.

Accordingly, we affirm the district court's judgment against the Hollanders and in favor of Presbyterian Hospital and Sandoz. We remand the Hollanders' claim against Sandoz, Ltd., so that it may be dismissed *without* prejudice.

Appendix A

I. BACKGROUND

On July 23, 1990, Ms. Hollander gave birth by cesarean section to a healthy baby boy at Presbyterian Hospital in Oklahoma City. Because Ms. Hollander did not want to breast feed her son, her obstetrician prescribed a fifteen day course of Parlodel, to be taken in two 2.5 mg doses per day.

Parlodel is manufactured by Sandoz. The drug's active ingredient is bromocriptine mesylate, a compound derived from ergot (a naturally occurring substance made from a fungus that attacks cereal grains). The compound blocks the production of prolactin, a hormone that triggers the secretion of milk in postpartum women. The Federal Drug Administration (FDA) approved Parlodel for the suppression of post-partum lactation in 1980, and approximately 9 million women in the United States have taken it for that purpose. *See Siharath v. Sandoz Pharms. Corp.*, 131 F. Supp. 2d 1347, 1349 (N.D. Ga. 2001) (discussing the history of Parlodel). Parlodel is also prescribed for several other disorders, including acromegaly (a disease caused by hypersecretion of the pituitary growth hormone), Parkinson's disease, and various diseases involving the excessive production of prolactin.

Ms. Hollander received her first dose of Parlodel at 6:00 p.m. on July 23, 1990. About two hours later, her blood pressure increased sharply to 180/90. On the following day, she received her second and third doses of Parlodel, and her blood pressure returned to the normal range. She continued to take two 2.5 mg doses of the drug each day. Presbyterian Hospital discharged her on July 27, 1990.

Appendix A

On the evening of July 28, 1990, Ms. Hollander complained of a severe headache. By the following morning, she could neither speak nor move her right side. At Presbyterian Hospital, a CT scan revealed that Ms. Hollander had suffered an intracerebral hemorrhage in the left basal ganglia area of her brain. Ms. Hollander's treating physicians were puzzled as to the cause. One of them noted that her stroke resembled those caused by hypertension but added that Ms. Hollander had no history of the disorder. Clinical information revealed no pregnancy-related disorders involving hypertension, such as eclampsia or preeclampsia.[1]

On August 1, 1990, Ms. Hollander's condition deteriorated. As a result, her physicians performed an emergency left frontal craniotomy and removed an intracerebral hematoma. Ms. Hollander slowly improved. She remained in the hospital for over three weeks and then transferred to a rehabilitation center.

The Hollanders filed this action against Sandoz, Sandoz, Ltd., and Presbyterian Hospital in May 1995 in the District Court for Oklahoma County. They alleged that Ms. Hollander's stroke was caused by Parlodel, that the drug was unreasonably dangerous to the ordinary consumer when used

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1. Preeclampsia involves the "[d]evelopment of hypertension with albuminuria or edema between the 20th week of pregnancy and the end of the 1st week postpartum." *The Merck Manual*, § 18 at 2057 (17th ed. 1999). "Albuminuria" refers to "the presence in the urine of serum albumin." *Dorland's Illustrated Medical Dictionary* at 42 (28th ed. 1994). Eclampsia involves "[c]onvulsive seizures or coma without other etiology occurring in the same time period." *The Merck Manual*, § 18 at 2057.

as a lactation suppressant, and that Sandoz, Sandoz, Ltd., and Presbyterian Hospital had failed to warn of the dangers of the drug. They further alleged that Ms. Hollander had suffered permanent injuries.

Presbyterian Hospital filed a motion to dismiss the Hollanders' claims, arguing that a hospital could not be held strictly liable for providing a drug prescribed by a doctor. The Oklahoma County District Court granted Presbyterian Hospital's motion to dismiss in an oral ruling at an August 25, 1995 hearing. It issued a written ruling on May 10, 1996.

Sandoz filed a notice of removal on May 10, 1996. The Hollanders then filed a motion to remand the case to the Oklahoma state court, which the district court denied. *See* Aplt's App. vol. I, at 116-17 (District Court Order, filed June 12, 1996). Subsequently, the court dismissed the Hollanders' claims against Sandoz, Ltd., reasoning that it was a holding company incorporated in Switzerland with its principal place of business there, that it had no office, manufacturing, distribution, or sales facilities in the United States, and that it did not advertise here. As a result, the court concluded that it lacked personal jurisdiction over Sandoz, Ltd., and it dismissed with prejudice the claims against the company. *See id.* at 354 (District Court Order, filed Dec. 17, 1996).

The dispute between the Hollanders and Sandoz involves issues that have been raised in other litigation as well as in regulatory proceedings. *See Kuhn v. Sandoz Pharms. Corp.*, 14 P.3d 1170, 1174 (2001) (describing a "decade-long

disagreement between Sandoz and the [FDA] concerning the use of Parlodel for the prevention of physiologic lactation"). In 1984 (four years after first approving the drug as a lactation suppressant), the FDA reported that "the labeling of Parlodel (bromocriptine) is being revised to reflect reports of postpartum hypertension, seizures, and cerebrovascular accidents." Aplt's App. vol. IV-B, at 2401-02 (*FDA Drug Bulletin*, vol. 14, no. 1, at 3- 4). The FDA explained that it had received seven reports of hypertension alone, seven reports of seizures, and three cases of cerebrovascular accidents (including one fatality). Because approximately 500,000 women had used Parlodel to suppress postpartum lactation, however, the significance of those reports was difficult to assess. The FDA expressly acknowledged that "[a] cause and effect relationship has not been established." *Id.*

Sandoz eventually modified the Parlodel package insert to include information about these cases. However, the company noted that hypertension, seizures, strokes, and myocardial infarctions regularly occur in postpartum women who are *not* treated with bromocriptine. Thus, it maintained, "the number of cases reported to Sandoz is less that one would expect even in the absence of any drug effect." *Id.* at 2448 (Letter from Sandoz's Executive Director of Sales, Aug. 20, 1987).

Over the next few years, the FDA continued to receive reports of adverse reactions to Parlodel. Sandoz commissioned a study by Epidemiologic Resources, Inc., regarding the relationship between Parlodel and strokes and seizures (the "ERI study"). *See* Aplt's App. vol. II-D, at 1361-1532 (Kenneth Rothman, et al., "An Epidemiologic Evaluation of the Possible Relation Between Bromocriptine, Puerperal Seizures and

Strokes," (Sept. 30, 1988));[2] *Siharath*, 131 F. Supp. 2d at 1356-57 (discussing the ERI study). Although the ERI study did not find a causal connection between strokes and seizures, the FDA concluded that the study failed to allay concerns regarding the drug's association with seizures and involved too few individuals to adequately characterize the risk of stroke.

The FDA further concluded that the possibility that Parlodel might cause serious adverse reactions in some patients outweighed the limited benefits associated with its use. As a result, it requested all manufacturers to remove the indication for lactation suppression from the Parlodel label. Initially, Sandoz refused to comply with the FDA's request, arguing that Parlodel should not be used routinely but should be available in specific circumstances recommended by physicians. Not satisfied with this position, the FDA initiated formal procedures for withdrawing its prior approval for the labeling of Parlodel. The FDA explained its position as follows:

> FDA now has new information suggesting that therapeutic use of bromocriptine for the prevention of physiological lactation may lead to serious adverse experiences, including death and paralysis, in a small but significant number of patients. Patients at high risk of experiencing these serious adverse experiences cannot be adequately predetermined. In light of the limited benefit of

2. The purpureum is "the period from the end of the third stage of labor until the involution of the uterus is complete, usually lasting 3 to 6 weeks." *Dorland's Illustrated Medical Dictionary* at 1386.

> using bromocriptine for the prevention of lactation, and the effectiveness and lack of serious adverse effects of conservative treatments such as breast binding with or without mild analgesics, the risk that bromocriptine may cause a serious adverse effect in a postpartum woman is unacceptable.
>
> Accordingly, the Director concludes that the potential risks associated with the use of bromocriptine for the prevention of physiological lactation outweigh its limited benefits and bromocriptine is no longer shown to be safe for use in preventing physiological lactation.

59 Fed. Reg. 43347, 43351 (Aug. 24, 1994). Sandoz then agreed to FDA's proposal to withdraw the indication for the suppression of postpartum lactation.

Following the FDA's approval of Parlodel as a lactation suppressant, professional medical journals began to publish reports regarding women who had suffered heart attacks and strokes after taking the drug. For example, one of the Hollanders' expert witnesses described two patients who had suffered from cardiac dysfunction, seizures, and cerebral vasospasm. *See* Kenneth Kulig, "Bromocriptine Associated Headache: Possible Life Threatening Sympathomimetic Intersection," *Obstetrics and Gynecology*, 72: 941(1991) (Aplt's App. vol. IV- B, at 2444-46). Another expert published case histories concerning women who had suffered from heart attacks. *See*, *e.g.*, Leslie Iffy, et al., "Acute Myocardial Infarction in the Puerperium in Patients Receiving

Bromocriptine," *American Journal of Obstetrics and Gynecology*, vol. 155, No. 2, at 371-72 (1986) (Aplt's App. vol. IV-D, at 2976-77). Medical researchers also published numerous articles reporting the effects of bromocriptine in animals. *See Siharath*, 131 F. Supp. 2d at 1366-69 (discussing animal studies), *Glastetter v. Novartis Pharms. Corp.*, 107 F. Supp. 2d 1015, 1037-1041 (E.D. Mo. 2000) (same), *aff'd*, 252 F.3d 986, 991 (8th Cir. 2001). Some of the studies involved dogs, rats, and pithed animals. *See id.*; *see also* Aplt's App. vol. I-A, at 369-376 (Sandoz's statement of material facts, filed July 15, 1999) (discussing animal studies). Some researchers concluded that, contrary to the Hollanders' allegations regarding the effect of bromocriptine on Ms. Hollander, the drug actually decreases blood pressure. *See, e.g.*, Saad Lahlou & Pierre Demenge, "Contribution of Spinal Dopamine Receptors to the Hypotensive Action of Bromocriptine in Rats," *Journal of Cardiovascular Pharmacology*, vol. 18, 317-323 (1991) (Aplt's App. vol. II-E, at 1646-54).

As the discussion in the scientific literature continued, the controversy over Parlodel made its way to the courts. In 1994, a Kentucky jury awarded $968,512 in compensatory damages and $1,000,000 in punitive damages to a woman who alleged that Parlodel had caused her stroke. *See* Aplt's App. vol. IV-A, at 2171 (Judgment in *Roberts v. Betts*, no. 89-CI-653-V, 25th Judicial Dist., Pulaski Cir. Ct., July 20, 1994). A Kentucky appellate court affirmed that judgment in an unpublished opinion. *See id.* at 2175-78. In contrast to the *Roberts* case, several recent decisions have rejected claims that Parlodel has caused strokes and heart attacks when prescribed as a post-partum lactation suppressant, concluding

that the scientific evidence supporting these claims was not sufficiently reliable under *Daubert*.[3] However, several other decisions have reached the opposite conclusion.[4] *See generally* Mark Hansen, "When Expert Testimony Fails the Test: District Courts Disagree on what Defines Causation Evidence in Drug Disability Cases," 88 *ABA Journal* 22 (Jan. 2002) (stating that "[an] Alabama magistrate's decision brought to eight the number of products liability suits over Parlodel that have survived a so-called *Daubert* challenge to the admissibility of the plaintiffs' causation evidence [b]ut [an] Illinois judge's ruling — tantamount to an order of summary judgment for the defense — marked the seventh trial or appellate decision to exclude such evidence").

In support of their contention that Parlodel caused Ms. Hollander's stroke, the Hollanders relied primarily on the testimony of three experts: (1) Dr. Kenneth Kulig, a physician who is board-certified in toxicology and emergency

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3. *See Glastetter v. Novartis Pharms. Corp.*, 252 F.3d 986, 989 (8th Cir. 2001); *Caraker v. Sandoz Pharms. Corp.*, 172 F. Supp. 2d 1046 (S.D. Ill. 2001); *Siharath*, 131 F. Supp. 2d 1347 (N.D. Ga. 2001); *Brumbaugh v. Sandoz Pharm. Corp.*, 77 F. Supp. 2d 1153, 1155, (D. Mont. 1999).

4. *See Brasher v. Sandoz Pharms. Corp.*, 160 F. Supp. 2d 1291 (N.D. Ala. 2001); *Globetti v. Sandoz Pharms. Corp.*, 111 F. Supp. 2d 1174 (N.D. Ala. 2000); Aplt's App. vol. V, at 3184-3213 (Tr. of unpublished ruling in *Kittelson v. Sandoz Pharms. Corp.*, No. 98-2277 (D. Minn. March 2, 2000)) (denying motion to exclude scientific testimony as unreliable); *Kuhn*, 14 P.3d at 1179-85 (applying the test for admissibility set forth in *Frye v. United States*, 293 F. 1013 (D.C. Cir. 1923) and concluding that there were genuine issues of material fact as to whether Parlodel caused a patient's death).

medicine and who has served as the Chairman of the Pharmacy and Therapeutics Committee and Director of the Porter Regional Toxicology Center at Porter Adventist Hospital in Denver, Colorado, and as an associate clinical professor in the Division of Emergency Medicine and Trauma in the Department of Surgery at the University of Colorado Health Sciences Center; (2) Dr. Leslie Iffy, M.D., a professor in the Department of Obstetrics and Gynecology of the University of Medicine and Dentistry of New Jersey; and (3) Dr. Pedro A. Jose, M.D., Ph.D., a Professor of Pediatrics, Physiology, and Biophysics at Georgetown University and an expert on the role of dopamine and dopaminergic drugs on the development of hypertension.

The parties offered deposition testimony, affidavits, expert reports, and transcripts of testimony from other cases involving Parlodel. In general, the experts' theory was that in certain women, Parlodel causes vasoconstriction (a narrowing of the blood vessels) and hypertension (high blood pressure). Vasoconstriction and hypertension, the experts reasoned, can then cause strokes, as they did in the case of Ms. Hollander.

In his written report, Dr. Kulig explained that he had reviewed Ms. Hollander's medical records, medical literature regarding bromocriptine and other ergot alkaloids, FDA documents, and marketing, promotional and research material complied by Sandoz. He concluded that Ms. Hollander suffered "an intracerebral hemorrhage secondary to ergot induced vasospasm resulting in blood vessel rupture in her brain." Aplt's App. vol. II-A, at 652 (Dr. Kulig's Sept. 22, 1998 report, at 3). He added, "It is my opinion with a

reasonable degree of medical certainty that Mrs. Hollander's stroke was caused by the drug bromocriptine, and had the patient not been taking the drug, she would not have had a stroke." *Id.* at 653. According to Dr. Kulig, the fact that bromocriptine could cause strokes was well know to Sandoz at the time that Ms. Hollander began taking the drug. *Id.* at 652.

In an affidavit in another case involving Parlodel, Dr. Kulig provided a more detailed explanation as to how he had reached his conclusions. *See* Aplt's App. vol. II-E, at 1742-59 (Dr. Kulig's affidavit in *Railey v. Novartis Pharmaceuticals Corp.*, 94-1440 (C.D. Ill.)). He noted that bromocriptine is an ergot, "a class of drugs with known molecular structures and many common properties," including the tendency to cause vasoconstriction. *See id.* at 1745 (stating that "[o]ne needs only to look at the package inserts from Sandoz regarding other ergot alkaloids it manufactures to understand that vasoconstriction is indeed the core property of ergot alkaloids"). Bromocriptine differs from the naturally occurring ergot alkaloid alpha ergocriptine only in that the molecule has an additional bromine atom attached to the second carbon atom of the basic ergot ring. *See id.*

Dr. Kulig explained the significance of the structural differences between bromocriptine and other ergot alkaloids as follows:

> Although the adding of a bromine atom to the core nucleus makes the drug in some patients a vasodilator (the first dose may cause a precipitous

> fall in blood pressure, another fact that makes the drug unsafe in the post-partum period), it is misleading and inaccurate to suggest that the drug can never cause vasoconstriction or hypertension in any person. While the addition of a bromine atom to a very large organic molecule may change the pharmacokinetics and pharmacological dynamics of a drug, it would be unlikely to change the core properties of an ergot alkaloid from being a vasoconstrictor to a vasodilator in *all* cases. Clinical studies, epidemiologic evidence and adverse drug reaction experience with this drug indicates that vasoconstriction with bromocriptine unquestionably occurs, as would be expected based on the fact that it is an ergot that can cause ergotism.

Id. at 1745-46.

Dr. Kulig also discussed several other categories of evidence on which he had relied in forming his opinion. These included the pharmacological and toxicological properties of bromocriptine, studies of the relationship between bromocriptine and hypertension, and case reports concerning adverse reactions.

As to pharmacology, Dr. Kulig explained that bromocripitne is "a dopamine agonist." *Id.* In other words, the drug stimulates the release of dopamine, a neurotransmitter. Dr. Kulig added that bromocriptine is also a "dopamine-1 antagonist," inhibiting the effects of dopamine at specific "D-1" receptors. *Id.* According to Dr. Kulig, dopamine is a well known vasoconstrictor. However, activation of the "D-1" dopamine receptors results in vasodilation. Thus, the fact that

bromocriptine stimulates the release of dopamine and that it inhibits the D-1 dopamine receptors is consistent with the drug causing vasoconstriction.

Moreover, Dr. Kulig reported that bromocriptine "has a very long beta elimination half-life of about 50 hours." *Id.* at 1747. That means that a steady state is not achieved in someone taking the drug twice a day until about ten days after leaving the hospital. As a result, one would not expect women who have taken the drug to suppress post-partum lactation to develop hypertension and vasospasm until after their discharge from the hospital.

With regard to hypertension, Dr. Kulig referred to three studies. In the first, commissioned by Sandoz, nineteen percent of patients demonstrated increases in blood pressure after taking bromocriptine. In the second study, published by the FDA in 1984, six out of seven patients who developed hypertension while on bromocriptine regained normal blood pressure after they stopped taking the drug. Finally, a study by Dr. Dorothy Watson[5] found that women with pregnancy-induced hypertension had a higher incidence of post-partum hypertension after taking the drug than those women not receiving bromocriptine. *See id.* at 1748-49 (stating that "[t]his case control study provides important evidence that bromocriptine causes post-partum hypertension in women who had pregnancy-induced hypertension prior to delivery").

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5. Watson, D.I., et al., "Bromocriptine Mesylate for Lactation Suppression: A Risk for Postpartum Hypertension?" *Obstetrics and Gynecology*, 74(4): 573-576 (1989) (Aplt's App. vol. II-D, at 1596-97).

Finally, Dr. Kulig discussed the adverse reactions to bromocriptine that had been spontaneously reported to the FDA and Sandoz. These reactions included hypertension, seizures, strokes, and myocardial infarction. Although he acknowledged that these reports did not establish causation, he presented them as an important factor to be considered along with the other scientific evidence.

In addition to Dr. Kulig, the Hollanders also relied on the opinion of Dr. Leslie Iffy. *See* Aplt's App. vol. II-A, at 733-739 (Dr. Iffy's written report, July 25, 1997). Dr. Iffy concluded that there was "an overwhelming probability" that Ms. Hollander's stroke was caused by bromocriptine. *Id.* at 738. He listed five factors that supported his opinion: (1) Ms. Hollander had normal blood pressure during a prior pregnancy but displayed an episode of hypertension when she took Parlodel during her first childbirth; (2) she suffered episodes of hypertension during her second pregnancy and immediately after the birth of her second child; "[t]his being the case, she was predisposed for the hypertensive effect of bromocriptine"; (3) when she took Parlodel after the second pregnancy, her blood pressure increased, "in all probability a bromocriptine effect"; (4) "[t]he time of occurrence of the cerebral hemorrhage (sixth day postpartum) was highly characteristic of bromocriptine related catastrophic side effects"; and (5) "[a]part from her moderate smoking habit, the patient had no identifiable predisposing factors for cerebral hemorrhage[;][t]he absence of evidence of congenital defect at the site of the hemorrhage further emphasizes the lack of predisposing factors on the part of the patient." *Id.* Dr. Iffy added that, in his view, Sandoz was aware of the dangers of Parlodel at the time that Ms. Hollander suffered her stroke. *See id.* at 739.

The third expert on whom the Hollanders relied — Dr. Pedro Jose — set forth a more specific theory of causation. In his written report, Dr. Jose stated, "I think that the hypertension (which caused the stroke) is probably due to Parlodel; the hypertension would not have happened if Parlodel was not prescribed." Aplt's App. vol. II-A, at 842 (Dr. Jose's report, Jan. 23, 1998). Dr. Jose acknowledged that bromocriptine often decreases blood pressure. However, in deposition testimony he explained that in instances in which extra-cellular fluid volume is increased — as is the case in pregnancy — and in which the activity of the sympathetic nervous system is decreased, bromocriptine has the "paradoxical effect of increasing blood pressure." *Id.* at 801.

After conducting discovery, Sandoz filed a motion to exclude the opinion testimony offered by the Hollanders' experts on the grounds that the testimony was insufficiently reliable under *Daubert*. In the same motion, Sandoz requested the court to grant summary judgment in its favor. It argued that, in the absence of the unreliable opinion testimony, the Hollanders could not demonstrate that there were controverted issues of material fact on the issue of whether Parlodel caused Ms. Hollander's stroke.

The federal district court granted Sandoz's motion to exclude the Hollanders' expert testimony as well as its motion for summary judgment. *See Hollander*, 95 F. Supp. 2d at 1235-39. The court set forth four reasons in support of its evidentiary ruling.

First, the court observed that the Hollanders' experts were unable to explain the physiological mechanism by which

Parlodel caused vasoconstriction and ensuing hypertension and strokes. The court explained that "Dr. Kulig could only list possible mechanisms for Parlodel causing hypertension," that "Dr. Jose could not cite any studies or tests that proved his hypothesis that bromocriptine might cause high blood pressure," and that "Dr. Iffy also classified his opinion that Parlodel caused Mrs. Hollander's stroke as being a hypothesis, which is not held by a medical degree of certainty." *See id.* at 1235-36 (internal quotation marks omitted).

Second, the court reasoned that the kinds of case reports on which the Hollanders relied have been repeatedly rejected as a scientific basis for establishing causation. It stated: "The problems with case reports and adverse drug experience reports were acknowledged by Dr. Iffy — because they are not controlled studies and do not eliminate confounding variables, the reported effect or injury could be due to some other cause than Parlodel." *See id.* at 1237.

Third, the court found that the fact that bromocriptine belongs to a class of compounds (ergot alkaloids) that have been shown to cause hypertension did not constitute reliable causation evidence. The court observed that the Hollanders had failed to refute Sandoz's evidence that "[t]he chemical diversity of ergot alkaloids corresponds to the diversity of the biological activities of these compounds." *Id.* at 1238 (internal quotation marks and emphasis omitted).

Fourth, the animal studies on which the Hollanders' experts relied were too dissimilar to the facts of this case. "The studies relied upon involved different drugs, did not test the systemic effect of the drug, some of the animals were anaesthetized,

and they were neither pregnant nor post-partum. . . . Doctors Jose and Kulig were unaware of any controlled animal studies in which bromocriptine caused an increase in blood pressure." *Id.* at 1238 (internal citations omitted).

In light of its conclusion that the Hollanders' opinion testimony was insufficiently reliable under *Daubert*, the district court briefly assessed the state of the record absent that testimony. It concluded that, without expert opinion testimony, the Hollanders could not demonstrate that Parlodel caused Ms. Hollander's stroke. The court therefore granted Sandoz's motion for summary judgment.

II. DISCUSSION

In this appeal, the Hollanders primarily challenge the district court's assessment of their evidence that Parlodel caused Ms. Hollander's stroke. In particular, they challenge both the district court's application of *Daubert* to exclude their expert opinion testimony and the district court's assessment of the record absent that testimony. They maintain that "[w]hether or not the experts are allowed to give their ultimate opinion, there is sufficient evidence that a jury could find in [their] favor on the issue of causation." Aplt's Br. at 28. The Hollanders also present several other challenges to the district court's rulings.

We begin our analysis by addressing the Hollanders' argument that the district court lacked subject matter jurisdiction and therefore erred in denying their motion to remand the case to the Oklahoma state court. Because we conclude that the federal district court had subject matter

jurisdiction, we then turn to the Hollander's arguments regarding scientific evidence. Finally, we address their argument that the district court erred in dismissing their claims against Sandoz, Ltd., with prejudice.

A. Jurisdiction

Focusing on several alleged defects in the removal procedure, the Hollanders argue that the federal district court erred in denying their motion to remand. As a result, they contend, that court lacked jurisdiction to adjudicate the case, and the judgment in favor of the defendants should be vacated so that the case may be heard in the Oklahoma state court.

In light of the Supreme Court's decision in *Caterpillar, Inc. v. Lewis*, 519 U.S. 61 (1996), we need not address the Hollanders' specific arguments. In *Caterpillar*, the Court held that "a district court's error in failing to remand a case improperly removed is not fatal to the ensuing adjudication if federal jurisdictional requirements are met at the time judgment is entered." *Id.* at 64; *see also Feichko v. Denver & Rio Grande W. R.R. Co.*, 213 F.3d 586, 590-91 (10th Cir. 2000) (discussing *Caterpillar*). The Court reasoned that, despite deficiencies in the removal process, "[to] wipe out the adjudication postjudgment, and return to state court a case now satisfying the federal jurisdictional requirements, would impose an exorbitant cost on our dual court system, a cost incompatible with the fair and unprotracted administration of justice." *Caterpillar*, 519 U.S. at 77.

Here, as the defendants observe, complete diversity existed between the remaining parties at the time that the federal district court entered judgment: the Hollanders resided in Arkansas and the defendant Sandoz was a Delaware corporation with its

principal place of business in New Jersey. Thus, the alleged deficiencies in the removal procedure do not divest the district court of subject matter jurisdiction. We therefore proceed to the merits.

B. Admissibility of the Hollanders' Experts' Testimony Under Daubert

Rule 702 of the Federal Rules of Evidence provides:

> [i]f scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

Fed. R. Evid. 702.

In *Daubert*, the Supreme Court concluded that Rule 702 superseded the "general acceptance" standard for the admissibility of scientific evidence first set forth in *Frye*, 293 F. at 1014.[6] Under *Daubert*, when faced with a proffer of expert scientific testimony, a district court "must determine at the

6. The *Frye* test required district courts to exclude evidence when the underlying scientific principles were not "sufficiently established to have gained general acceptance in the particular field in which [they belong]." *Frye*, 293 F. at 1014.

outset, pursuant to [Fed. R. Evid.] 104(a), whether the expert is proposing to testify to (1) scientific knowledge that (2) will assist the trier of fact to understand or determine a fact in issue." *Daubert*, 509 U.S. at 592. Thus, under *Daubert*, the district court performs an important gatekeeping role in assessing scientific evidence. *See Macsenti v. Becker*, 237 F.3d 1223, 1230-34 (10th Cir. 2001) (discussing the district court's gatekeeping function under *Daubert*).

The *Daubert* standard ensures that the proffered evidence is both "reliable" and "relevant." *See Daubert*, 509 U.S. at 589. Reliability is determined by assessing "whether the reasoning or methodology underlying the testimony is scientifically valid." *Id.* at 592-93. Relevance depends upon "whether [that] reasoning or methodology properly can be applied to the facts in issue." *Id.* at 593.

We review the district court's application of *Daubert* to exclude expert opinion evidence for an abuse of discretion. *See General Electric v. Joiner*, 522 U.S. 136, 143 (1997); *Mitchell v. Gencorp Inc.*, 165 F.3d 778, 780 (10th Cir. 1999). Thus, we must afford *substantial deference* to the district court's application of *Daubert*. *See Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999) ("the trial judge must have considerable leeway in deciding in a particular case how to go about determining whether particular expert testimony is reliable"); *Joiner*, 522 U.S. at 143 (noting that the court of appeals "failed to give the trial court the deference that is the hallmark of abuse-of-discretion review"). Under the abuse of discretion standard, "a trial court's decision will not be disturbed unless the appellate court has a definite and firm conviction that the lower court made a clear error of judgment

or exceeded the bounds of permissible choice in the circumstances." *McEwen v. City of Norman, Okla.*, 926 F.2d 1539, 1553-54 (10th Cir. 1991); *see also Summers v. Missouri Pacific R.R. System*, 132 F.3d 599, 603 (10th Cir. 1997) (stating that, under the abuse of discretion standard, "[w]e will not disturb the trial court's determination 'absent a distinct showing it was based on a clearly erroneous finding of fact or an erroneous conclusion of law or manifests a clear error of judgment' ").

Here, the Hollanders focus on the district court's application of the "reliability" prong of the *Daubert* inquiry. They invoke two methods of causation analysis: one promulgated by Sandoz's Drug Monitoring Center and the other set forth by a professor of medical statistics, Sir Austin Bradford Hill. *See* Aplt's App. vol. IV-B, at 2378-79 (Sandoz's classifications of evidence of causation); vol. IV-D, at 2949-52 (Bradford Hill, "The Environment and Disease: Association or Causation?," *Proceedings of the Royal Society of Medicine*, vol. 58 no. 5 (May 1965)).[7]

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7. Under the Sandoz scheme, there are four main categories of causation: (a) not related; (b) remote; (c) probable; and (d) definite. The Hollanders focus on the standard for "probable" causation.

An adverse reaction is considered to be "probably related to a drug" if the reaction: (1) "occurs within a reasonable time interval following the administration of the drug"; (2) "could not readily be attributed to the patient's clinical condition/underlying disease, concomitant therapy, or to environmental or toxic factors"; (3) "follows a known pattern of response to the drug"; and (4) "disappears or improves following cessation of treatment or dose reduction." *See* Aplt's App. vol. IV-B, at 2378-79.

(Cont'd)

Relying primarily on Dr. Kulig's testimony, the Hollanders maintain that his opinion that Parlodel caused Ms. Hollander's stroke comports with these general standards of causation analysis. Accordingly, they reason, Dr. Kulig's testimony is sufficiently scientific to be admissible under *Daubert*. *See* Aplt's Br. at 24 ("[I]t cannot be gainsaid that Dr. Kulig's methodology — how he takes the information available and analyzes it in a scientific manner — is good science and would be helpful to a jury of laymen.").

Additionally, the Hollanders note that Dr. Kulig criticized some of Sandoz's own evidence on scientific grounds. They point to his testimony that the studies invoked by Sandoz do not demonstrate that there is an increased risk of stroke in the post-partum period generally. As a result, they maintain, the evidence is disputed as to whether Ms. Hollander's stroke may be explained by this generally increased risk during the post-partum period, as Sandoz contends, rather than by her taking Parlodel.

Finally, the Hollanders contend that Drs. Kulig, Iffy, and Jose applied the methodology generally employed by experts in the relevant fields. Thus, by relying on scientific principles, professional publications, animal studies, differential diagnoses, and case reports, these experts did what *Daubert* requires: they

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Sir Bradford Hill sets forth nine factors that should be considered "before deciding that the most likely interpretation [of the association] is causation." These factors are: strength, consistency, specificity, temporality, dose response, biological plausibility, coherence, experimental evidence and analogy. *See* Aplt's App. vol. IV D, at 2949-52 (Bradford Hill paper); vol. II-E, at 1751-55 (Dr. Kulig's affidavit). Dr. Kulig applies the Bradford Hill criteria in reaching his opinion that Parlodel caused Ms. Hollander's stroke.

grounded their conclusions in "the methods and procedures of science" rather than "subjective belief or unsupported speculation." *Daubert*, 509 U.S. at 590.

In order to assess the Hollanders' argument, we begin with an overview of the standards for reliability under *Daubert* and its progeny. Then we turn to an examination of the scientific opinion evidence at issue here.

1. Scientific Reliability Under Daubert

Under *Daubert*'s reliability prong, "an inference or assertion must be derived by the scientific method . . . [and] must be supported by appropriate validation — i.e. 'good grounds,' based on what is known." *Id.* The Supreme Court listed four nonexclusive factors that the trial court may consider in assessing reliability: (1) whether the opinion at issue is susceptible to testing and has been subjected to such testing; (2) whether the opinion has been subjected to peer review; (3) whether there is a known or potential rate of error associated with the methodology used and whether there are standards controlling the technique's operation; and (4) whether the theory has been accepted in the scientific community. *See id.*

The list is not exclusive, and district courts applying *Daubert* have broad discretion to consider a variety of other factors. *See Kumho Tire*, 526 U.S at 150 ("[W]e can neither rule out, nor rule in, for all cases and for all time the applicability of the factors mentioned in *Daubert*, nor can we now do so for subsets of cases categorized by category of expert or by kind of evidence. Too much depends upon the particular circumstances of the particular case at issue."). Generally, the district court should focus on the experts' methodology rather than the conclusions that they generate. *See Daubert*, 509 U.S. at 595.

However, the experts' conclusions are not immune from scrutiny: "A court may conclude that there is simply too great an analytical gap between the data and the opinion proffered." *Joiner*, 522 U.S. at 147 ("[N]othing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert."). Regardless of the specific factors at issue, the purpose of the *Daubert* inquiry is always the same: "[t]o make certain that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field."[8] *Kumho Tire*, 526 U.S. at 152.[9]

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8. As Justice Breyer has observed, the requirement that the district court assess reliability and relevance under *Daubert* "will sometimes ask judges to make subtle and sophisticated determinations about scientific methodology and its relation to the conclusions an expert witness seeks to offer — particularly when a case arises in an area where the science itself is tentative or uncertain, or where testimony about general risk levels in human beings or animals is offered to prove individual causation." *Joiner*, 522 U.S. at 147-48, 118 S. Ct. 512 (Breyer, J., concurring). Even though judges usually do not have the formal scientific training to assist them in making these decisions, there are Rules of Evidence and Civil Procedure that may assist them in making the necessary determinations. "Among these techniques are an increased use of pretrial conference authority [pursuant to Fed. R. Civ. P. 16] to narrow the scientific issues in dispute, pretrial hearings where potential experts are subject to examination by the court, and the appointment of special masters and specially trained law clerks." *Id.* at 149 (citations omitted).

9. Judge Posner has expressed a similar view. "When the Supreme Court in *Daubert* told judges to distinguish between real

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Appendix A

2. The Hollanders' Scientific Evidence

We assess the Hollanders' challenge to the district court's *Daubert* ruling by examining the opinions of their three primary experts: Drs. Kulig, Iffy, and Jose. As to each expert, we must assess the grounds that they provide for their opinion that Parlodel causes stroke, asking whether those grounds involve "the methods and procedures of science," *Daubert*, 509 U.S. at 590, and "the level of intellectual rigor of the expert in the field." *Kumho Tire*, 526 U.S. at 152.

In doing so, we note that the scope of our review is quite narrow: we may reverse the district court's ruling only if we conclude that it abused its discretion in applying *Daubert* to exclude opinions of the Hollanders' experts. Because the district court has discretion to consider a variety of factors is assessing reliability under *Daubert*, and because, in light of that discretion, there is not an extensive body of appellate case law defining the criteria for assessing scientific reliability, we are limited to determining whether the district court's application of the *Daubert* manifests a clear error of judgment or exceeds the bounds of permissible choice in the circumstances. *See McEwen*, 926 F.2d at 1553-54 (discussing appellate review for an abuse of discretion). Thus, when coupled with this deferential standard of review, *Daubert*'s

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and courtroom science, it was not with the object of discovering the essence of "science," if there is such an essence. The object . . . was to make sure that when scientists testify in court they adhere to the same standards of intellectual rigor that are demanded in their professional work." *Rosen v. C G Corp.*, 78 F.3d 316, 318 (7th Cir. 1996).

effort to safeguard the reliability of science in the courtroom may produce a counter-intuitive effect: different courts relying on the essentially the same science may reach different results. *See generally Federal Judicial Center, Reference Manual on Scientific Evidence* 27 (2d ed. 2000) (observing that, in light of the abuse of discretion standard of review for *Daubert* determinations of reliability, "in theory judges are free to select different procedures and apply different factors to a particular expert or type of expertise than their colleagues do in the same district or circuit" and that "[a]s a consequence, similar cases could be resolved differently on the basis of inconsistent determinations about admissibility"); *see also Brasher*, 160 F. Supp. 2d at 1298 n.17 (observing that the Eighth Circuit's decision in *Glastetter*, 252 F.3d at 989-92, affirming the exclusion of Parlodel evidence as unreliable "does not necessarily [establish] that an inconsistent holding by this court would constitute an abuse of discretion").[10]

a. Similarity to other ergot alkaloids

We begin our analysis with Dr. Kulig's testimony that bromocriptine is an ergot alkaloid. According to Dr. Kulig, this fact supports his theory that bromocriptine causes vasoconstriction.

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10. Conflicting decisions in the district courts regarding the reliability of opinion testimony about Parlodel further illustrate this point. *Compare Siharath*, 131 F. Supp. 2d 1347 (evidence regarding Parlodel's adverse effects unreliable); *and Brumbaugh*, 77 F. Supp. 2d 1153 (same); *with Brasher*, 160 F. Supp. 2d 1291 (Parlodel evidence reliable); *and Globetti v. Sandoz Pharms., Corp.*, 111 F. Supp. 2d 1174 (N.D. Ala. 2000) (same).

As the district court observed, neither Dr. Kulig nor the Hollanders' other experts disputed the fact that bromocriptine has a different chemical structure than ergot alkaloids known to cause vasoconstriction. Moreover, neither Dr. Kulig nor the Hollanders' other experts disputed the scientific literature stating that small differences in chemical structure may produce substantial differences in physiological effects.

In light of these considerations, several courts have agreed with the district court's conclusion that the fact that bromocriptine is an ergot alkaloid does not constitute reliable scientific evidence that it causes vasoconstriction and associated adverse reactions like heart attacks and strokes. *See Glastetter*, 252 F.3d at 990 ("[T]his generic assumption that bromocriptine behaves like other ergot alkaloids carries little scientific value. Even minor deviations in molecular structure can radically change a particular substance's properties and propensities.");[11] *Brumbaugh*, 77 F. Supp. 2d at 1156 ("Testimony extending general conclusions about similar drugs does not meet *Daubert's* requirement of reliability."); *Siharath*, 131 F. Supp. 2d at 1363-65 (finding a lack of reliable evidence that bromocriptine acts like other ergot alkaloids). Moreover, in a similar case, this circuit has rejected the argument that one chemical's resemblance to another known to have deleterious effects constituted reliable causation evidence. *See Mitchell*, 165 F.3d at 782 ("Missing

11. The Eighth Circuit also noted that "one leading treatise on medical toxicology concludes that bromocriptine has no vasoconstrictive properties." *Glastetter*, 252 F.3d at 990 (emphasis in original) (citing Matthew J. Ellenhorn, *Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning* 1879, table 74-23 (2d ed. 1997)).

from [the plaintiff's evidence] is additional testimony explaining what these similarities are and how the similarities cause the human body to respond to Defendant's chemicals in a manner similar to benzene.").

These decisions support the district court's analysis. Accordingly, the district court did not abuse its discretion in finding that bromocriptine's similarity to other ergot alkaloids constituted an unreliable basis on which to conclude that the drug causes vasoconstriction and ensuing adverse effects like Ms. Hollander's stroke.

b. Pharmacology of bromocriptine

In important respects, the Hollanders' experts' discussion of the specific pharmacological properties of bromocriptine is similarly speculative. For example, Dr. Kulig's affidavit refers to the drug's known effects on dopamine and serotonin, and notes that these neurotransmitters are known to trigger vasoconstriction and vasospasm. However, although he states that the effect of Parlodel on serotonin receptors "has been demonstrated in company studies," Aplt's App. vol. II E, at 1747, Dr. Kulig provides no details on the methodology or conclusions of these studies. Moreover, the mere fact that Parlodel acts on serotonin and dopamine receptors does not establish that Parlodel itself, as opposed to some other agent that triggers either the release of these neurotransmitters or some other physiological mechanism, causes vasoconstriction, hypertension, and stroke.

The testimony of Dr. Jose (the expert on peripheral dopamine receptors) reveals similar deficiencies. Although

he presented an elegant theory of the way in which bromocriptine might have the paradoxical effect of causing vasoconstriction and increased blood pressure, he acknowledged that there were a number of animal studies that concluded that bromocriptine *decreases* blood pressure. Dr. Jose attempted to distinguish these studies by observing that the specific conditions that he had posited as necessary to trigger the paradoxical effects of bromocriptine were not present. However, he acknowledged that his thesis had not been tested. *See* Aplt's App. vol. II-A, at 802 ("I have bits and pieces proving that bromocriptine can increase sodium reabsorption, bits and pieces that can show that bromocriptine can decrease blood flow; but to put all of them together [to demonstrate that bromocriptine can cause high blood pressure] no, that has not been tested."). Accordingly, the district court did not exercise manifestly unreasonable judgment in concluding that the opinions of the Hollanders' experts did not meet the *Daubert* reliability standard insofar as those opinions were based on the pharmacology of bromocriptine.

c. Studies of hypertension

Both Dr. Kulig and Dr. Iffy relied on studies regarding the relationship between bromocriptine and hypertension. Dr. Kulig referred to a 1981 study commissioned by Sandoz in which women received the drug to treat amennorrhea-galactorrhea syndrome.[12] Dr. Kulig states that nineteen

12. Amenorrhea refers to an "absence or abnormal stoppage of the menses." *See Dorland's Illustrated Medical Dictionary* 55. Galactorrhea is the "excessive or spontaneous flow of milk" or the "persistent secretion of milk irrespective of nursing." *Id.* at 672.

percent of those women reported increases in blood pressure. Both experts invoke a study by D.I. Watson, which concluded that women with pregnancy-induced hypertension who then took bromocriptine after giving birth had a higher incidence of postpartum hypertension than women who did not receive the drug.[13]

Again, it is not an abuse of discretion to conclude that there is "simply too great an analytical gap" between these studies and the experts' conclusion that Parlodel caused Ms. Hollander's stroke. *See Joiner*, 522 U.S. at 146. The studies in question do not directly address the relationship between Parlodel and stroke. Moreover, the Hollanders presented no expert analysis as to how one might extrapolate from bromocriptine's effect on a small group of women with amennorrhea-galactorrhea syndrome to determine the effect that the drug would have on women like Ms. Hollander who took the drug as a postpartum lactation suppressant.

As to the Watson study, Dr. Iffy admitted that it did not claim a "high degree of reliability." Aplt's App. vol. II-A, at 698. Dr. Iffy acknowledged that, under the study's criteria for determining which women had pregnancy-induced hypertension, Ms. Hollander herself would not qualify. *Id.* Thus, she was not in the class of patients whose blood pressure increased after taking Parlodel.

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13. D.I. Watson, et al., *supra, Obstetrics and Gynecology*, 74(4): 573-576 (Aplt's App. vol. II-D, at 1596 97).

Appendix A

d. Animal Studies

According to the Hollanders' experts, there are certain animal studies that also provide evidence that bromocriptine may cause vasoconstriction, hypertension, and stroke. These studies included those performed on isolated veins, on animals that were unconscious, and on pithed animals. Many involved large doses of bromocriptine, relatively much greater than the doses taken by Ms. Hollander.

Several recent decisions considering these studies have agreed with the district court's analysis. The studies suggest only that bromocriptine may act as a vasoconstrictor in very specific circumstances in certain kinds of animals; the studies do not constitute reliable evidence that bromocriptine causes strokes. *See Glastetter*, 252 F.3d at 991 (noting that one of the plaintiff's experts concluded that "not a single animal study had ever concluded that [intracerbral hemorrhage] was associated with bromocriptine"); *Caraker v. Sandoz Pharms. Corp.*, 172 F. Supp. 2d 1046, 1050-51 (S.D. Ill. 2001) (noting that "some [studies] involved animals that had a steel rod injected down their spinal cord to destroy it so the animal has no intact nervous system, some involved bromocriptine's reaction locally (*e.g.*, in a single isolated vein of an animal) as opposed to a systemic administration; and some were poorly documented"); *Siharath*, 131 F. Supp. 2d at 1367-69 (discussing three animal studies in detail and concluding that they did not constitute a reliable basis for experts' opinions that Parlodel caused the plaintiff's stroke).

In light of these characteristics of the animal studies, the district court's conclusion that they were unreliable does

not "exceed[ ] the bounds of permissible choice in the circumstances." *McEwen*, 926 F.2d at 1553-54. We therefore discern no abuse of discretion in the court's analysis.

e. Case studies and differential diagnosis

The next methodologies employed by the Hollanders' experts present a closer question. "Differential diagnosis" refers to the process by which a physician " 'rule[s] in' all scientifically plausible causes of the plaintiff's injury. The physician then 'rules out' the least plausible causes of injury until the most likely cause remains." *Glastetter*, 252 F.3d at 989 (8th Cir. 2001). The remaining cause is the expert's conclusion. *Id.* In conducting a differential diagnosis, physicians often use case reports — "a doctor's account of a particular patients' reaction to a drug or other stimulus, accompanied by a description of the relevant surrounding circumstances." *Id.*

Here, Drs. Kulig, Iffy, and Jose performed a differential diagnosis, reviewing Ms. Hollander's medical history and medical records, excluding other causes of her stroke, and then attributing the stroke to Parlodel. They relied in part on case reports, both those filed with the FDA and those published in the professional literature. Dr. Kulig expressed the view that the onset of Ms. Hollander's initial symptom (i.e., developing a headache several days after giving birth) and the timing of her stroke (several days after her discharge from the hospital) fit a general pattern seen in patients suffering adverse reactions to Parlodel and was also consistent with the pharmokinetics of the drug.

Appendix A

With regard to differential diagnoses, courts have reached contrasting conclusions as to reliability under *Daubert*. *Compare Westberry v. Gislaved Gummy AB*, 178 F.3d 257, 262-66 (4th Cir. 1999) (holding that "[a] reliable differential diagnosis provides a valid basis for an expert opinion on causation" and concluding that the district court did not abuse its discretion in admitting a physician's opinion testimony based on differential diagnosis) *with Glastetter*, 252 F.3d at 989 (holding that a district court did not abuse of discretion in excluding a differential diagnosis that was "scientifically invalid"); *see also Federal Judicial Center*, *Reference Manual on Scientific Evidence* 34 (2d. ed. 2000) (noting that "[j]udges disagree on whether a physician relying on the methodology of clinical medicine can provide adequate proof of causation in a toxic tort action"). Courts have also reached contrasting conclusions as to the reliability of case reports. *Compare Glaser v. Thompson Med. Co.*, 32 F.3d 969, 975 (6th Cir. 1994) (holding that the district court abused its discretion in excluding physician's opinion testimony based in part on case reports) *with Casey v. Ohio Med. Prods.*, 877 F. Supp. 1380, 1385 (N.D. Cal. 1995) (stating that "case reports are not reliable scientific evidence of causation, because they simply described reported phenomena without comparison to the rate at which the phenomena occur in the general population or in a defined control group; do not isolate and exclude potentially alternative causes; and do not investigate or explain the mechanism of causation"); *see generally Federal Judicial Center*, *Reference Manual on Scientific Evidence* 475 (noting that "[c]ausal attribution based on case studies must be regarded with caution" but that "such studies may be carefully considered in light of other information available, including toxicological data,"

and citing cases reaching contrasting conclusions on their admissibility under *Daubert*).[14] Our circuit does not appear to have addressed the reliability of differential diagnosis and case reports under *Daubert*.

In the instant case, the district court made short shrift of the Hollanders' experts' differential diagnoses and reliance on case reports. The court stated that "[b]ecause of their limitations, case reports have been repeatedly rejected as a scientific basis for a conclusion regarding causation." *Hollander*, 95 F. Supp. 2d at 1237.

Because the *Daubert* reliability inquiry is case-specific, we need not address, in general terms, the reliability of differential diagnoses and case reports. *See Kumho Tire*, 526 U.S. at 150. Instead, we must only decide whether the district court abused its discretion by characterizing the specific diagnoses and case reports at issue here as unreliable under *Daubert*.

Again, we conclude that the district court did not abuse its discretion. In many of the decisions in which a differential diagnosis has been deemed reliable, the party relying on the

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14. The conflicting views of the reliability of differential diagnosis are apparent in the Parlodel cases too. *Compare Brasher*, 160 F. Supp. 2d at 1296 (concluding that differential diagnosis constitutes a reliable methodology under *Daubert*) and *Globetti*, 111 F. Supp. 2d at 1178 (characterizing differential diagnosis as "a well-recognized and widely-used technique relied on by medical clinicians worldwide to identify and isolate the causes of disease") with *Glastetter*, 252 F.3d at 1362 (concluding that differential diagnosis and case reports did not establish reliable proof of causation), *and Siharath*, 131 F. Supp. 2d at 1361-63 (same).

diagnosis has offered independently reliable evidence that the allegedly dangerous drug or substance had harmful effects. *See, e.g.*, *Zuchowicz v. United States*, 140 F.3d 381, 385-87 (2d Cir. 1998) (affirming admission of differential diagnosis based in part on scientific articles regarding the effects of a drug); *Kennedy v. Collagen Corp.*, 161 F.3d 1226, 1228-30 (9th Cir. 1998) (holding that the district court abused its discretion in excluding expert opinion based on differential diagnosis when the diagnosis was supported by scientific and clinical studies regarding the connection between collagen and autoimmune disorders). That is not the case here. In order to "rule in" Parlodel as a scientifically plausible cause of Ms. Hollander's stroke, the Hollanders' experts would need to present reliable evidence that the drug can cause strokes, and for the reasons we have discussed, the district court did not abuse its discretion in concluding that the experts did not do so. *See Glastetter*, 252 F.3d at 989 (affirming the district court's exclusion of a differential diagnosis); *cf. Siharath*, 131 F. Supp. 2d at 1362-63 ("[A] fundamental assumption underlying this method is that the final, suspected 'cause' remaining after this process of elimination must actually be capable of causing the injury. That is, the expert must 'rule in' the other suspected cause as well as 'rule out' other possible causes. And, of course, expert opinion on this issue of general causation must be derived from scientifically valid methodology.") (internal quotation marks omitted).

We take a similar view of the case reports regarding other women suffering various injuries after taking Parlodel. Many of these case reports contain only limited information regarding the medical histories of the patients and the nature

of the injuries they suffered. In addition, given the large number of women who took Parlodel and the variety of possible causes for many of these injuries, it was not unreasonable for the district court to characterize the reports as unreliable evidence of causation. *See Siharath*, 131 F. Supp. 2d at 1361 (noting that "case reports . . . do not isolate and exclude potentially alternative causes; and do not investigate or explain the mechanism of causation" and that, as to Parlodel, "the modest number of case reports associating the drug with stroke or even postpartum hypertension is not what would be expected if there was a significant increased risk") (internal quotation marks omitted).

In holding that the district court did not abuse its discretion in excluding the particular differential diagnoses and case reports submitted by the Hollanders, we emphasize that, in other litigation, there may well be differential diagnoses and case reports that do not suffer from the same deficiencies noted by the district court here. For example, if the case reports in this record contained more detailed information about other women who suffered strokes and heart attacks after taking Parlodel, and if there were a substantially larger number of such detailed reports, that information might have provided support for the theories of Drs. Kulig, Iffy, and Jose. In that instance, a district court might well be justified in finding opinion testimony like that of Drs. Kulig, Iffy, and Jose reliable under *Daubert*. *See Caraker*, 172 F. Supp. 2d at 1050 (stating that "an overwhelming amount of case reports of a temporal proximity between a very specific drug and a very specific adverse event might . . . be enough to make a general causation conclusion sufficiently reliable" but adding that "[i]n this case, however, we have a scant number of case reports").

Moreover, as the Eighth Circuit has written:

> [W]e do not believe that a medical expert must always cite published studies on general causation in order to reliably conclude that a particular object caused a particular illness. The first several victims of a new toxic tort should not be barred from having their day in court simply because the medical literature, which will eventually show the connection between the victims' condition and the toxic substance, has not yet been completed. If a properly qualified medical expert performs a reliable differential diagnosis through which, to a reasonable degree of medical certainty, all other possible causes of the victims' condition can be eliminated, leaving only the toxic substance as the cause, a causation opinion based on that differential diagnosis should be admitted.

Turner v. Iowa Fire Equip. Co., 229 F.3d 1202, 1209 (8th Cir. 2000) (internal quotation marks omitted); *see also Westberry*, 178 F.3d at 262 (holding that a reliable differential diagnosis alone may provide a valid foundation for a causation opinion, even when no epidemiological studies, peer-reviewed published studies, animal studies, or laboratory data are offered in support of the opinion). However, in light of the deficiencies of the particular differential diagnoses and case reports in this record, the district court's analysis was not unreasonable.

Appendix A

f. Rechallenge and dechallenge reports

Ms. Hollanders' experts also presented several accounts of rechallenge and dechallenge. Rechallenge occurs when a patient is exposed to the same drug thought to have previously caused an adverse reaction. Dechallenge occurs when the drug is removed. As the Eighth Circuit has noted, rechallenge and dechallenge resemble controlled experiments in some ways, and thus may be more valuable than typical case reports. *Glastetter*, 252 F.3d at 990-91. Occasionally the results may appear quite dramatic. For example, one Sandoz employee described a rechallenge-dechallenge report as " 'the smoking gun' we have looked for so diligently." Aplt's App. vol. IV-B, at 2364.[15]

Nevertheless, by the Hollanders' account, there were only three such reports. *See* Aplt's Br. at 31. Of these three, only one involved vasoconstriction of the cerebral blood vessels.[16] Moreover, as to that incident, the only information to which the Hollanders' have directed us is a second-hand account by a Sandoz physician. Thus, the district court conclusion here — that there were too few of these reports for them to constitute reliable evidence of causation under *Daubert* —

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15. A physician reported to Sandoz that he had induced vasoconstriction of the cerebral blood vessels by administering small doses of Parlodel to a woman who had previously suffered a stroke after taking the drug. *See* Aplt's App. vol. IV-B, at 2364-65 (memorandum from Dr. William F. Westin, dated Sept. 17, 1987). There appears to be no further discussion of this report in the record.

16. One of the incidents involved the vasoconstriction of a coronary artery and another involved hypertension.

was not unreasonable. *Cf. Glastetter*, 252 F.3d at 990 (finding rechallenge and dechallenge data to be more potent proof of causation than did the district court but further concluding that the district court did not abuse its discretion in excluding it).

g. The Risks of Stroke in the Postpartum period

A linchpin of Sandoz's defense was that there is an increased risk of stroke in the postpartum period generally. Sandoz relied heavily on a study concluding that there is a 28.3 relative risk of stroke for women in the postpartum period, as compared with non-pregnant women. *See* Steven J. Kittner, et al., Pregnancy and the Risk of Stroke, *New Eng. J. Med.* 768-74 (1996) (Aplt's App. vol. II-C, at 1335-41).[17]

17. One authority explains the concept of "relative risk" as follows:

> [Relative risk] is defined as the ratio of the incidence rate (often referred to as incidence) of disease in exposed individuals to the incidence rate in unexposed individuals.
>
> . . . .
>
> The incidence rate of disease reflects the number of cases of disease that develop during a specified period of time divided by the number of persons in the cohort under study. Thus, the incidence rate expresses the risk that a member of the population will develop the disease within a specified period of time.
>
> For example, a researcher studies 100 individuals who are exposed to an agent and 200 who are not exposed. After one year, 40 of the exposed individuals are diagnosed as having a disease, and 20 of the unexposed individuals are

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Thus, according to Sandoz, Ms. Hollander's stroke could well have been the result of the increased risk to which all women

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(Cont'd)

> also diagnosed as having the disease. The relative risk of contracting the disease is calculated as follows:
>
> -The incidence rate of disease in the exposed individuals is 40 cases per year per 100 persons (40/100), or 0.4
>
> -The incidence rate of disease in the unexposed individuals is 20 cases per year per 200 persons (20/200), or 0.1.
>
> A relative risk of 4.0 indicates that the risk of disease in the exposed group is four times as high as the risk of disease in the unexposed group.
>
> . . . .
>
> Although a relative risk is a straightforward concept, care must be taken in interpreting it. Researchers should scrutinize their results for error. Error in the design of the study could yield an incorrect relative risk. Sources of bias and confounding should be examined. Whenever an association is uncovered, further analysis should be conducted to determine if the association is real or due to an error or bias. Similarly, a study that does not find an association between an agent and disease may be erroneous because of bias or random error.

Federal Judicial Center, Reference Manual on Scientific Evidence 348-49.

Thus, in the instant case, the study cited by Sandoz concluded that women in the postpartum period were 28.3 times more likely than non-pregnant women to have suffered a stroke.

are exposed during the postpartum period rather than an adverse reaction to Parlodel.

In the district court proceedings, the Hollanders challenged this argument primarily through the testimony of Dr. Kulig, who stated that the Kittner study (and others reaching similar conclusions about the risks of the postpartum period) did not control for bromocriptine use or for specific conditions that increase the risk of stroke, such as eclampsia. According to Dr. Kulig, when these factors are excluded, the Kittner study does not establish that there is an increased risk of stroke in the postpartum period.

The district court acknowledged Dr. Kulig's criticisms of the study. However, the court found that "the postpartum incidence of stroke is a factor that should be considered." *See Hollander*, 95 F. Supp. 2d at 1238 n.21.

The Hollanders now argue that the district court erred in its qualified affirmation of the Kittner study in the face of Dr. Kulig's critique of it. If this case required Sandoz to prove that there was an increased risk of stroke during pregnancy, we might agree. However, no such burden is imposed on Sandoz here. Instead, it is the Hollanders who have the burden of demonstrating the harmful effect of Parlodel. Accordingly, it was not unreasonable for the district court to conclude that Dr. Kulig's attack on the Kittner study did not constitute reliable evidence that Parlodel caused Ms. Hollander's stroke.

In summary, we agree with the court's assessment in *Siharath*: the Hollanders have done the best they could with the available data and the scientific literature. *See* 131

F. Supp. 2d at 1373. The data on which they rely might well raise serious concerns in conscientious clinicians seeking to decide whether the benefits of the drug outweigh its risks. However, in deriving their opinions that Parlodel caused Ms. Hollander's stroke from the various sources we have outlined, Drs. Kulig, Iffy, and Jose all made several speculative leaps. As a result, the district court did not abuse its discretion in excluding their testimony under *Daubert*.

C. Grant of Summary Judgment to Sandoz

In a related argument, the Hollanders maintain that, even if the district court did not abuse its discretion in excluding their experts' testimony, the court nevertheless erred in granting summary judgment to Sandoz.

According to the Hollanders, the following evidence demonstrates that there are controverted issues of material fact as to whether Parlodel caused her stroke: (1) the FDA's determination that Parlodel had not been shown to be safe when prescribed as a postpartum lactation suppressant; (2) the judgment entered against Sandoz in a case in Kentucky involving Parlodel; (3) incidents of dechallenge and rechallenge; (4) case reports; (5) studies of hypertension; (6) the fact that bromocriptine is an ergot; (7) animal studies; and (8) epidemiological studies.

We engage in de novo review of the district court's summary judgment ruling, applying the same standard as the district court under Fed. R. Civ. P. 56(c). *See Adler v. Wal-Mart Stores, Inc.*, 144 F.3d 664, 670 (10th Cir. 1998). Summary judgment is appropriate "if the pleadings, depositions, answers to interrogatories, and admissions on

file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to a judgment as a matter of law." Rule 56(c). We view the facts and the reasonable inferences to be drawn from them in the light most favorable to the nonmoving party. *Adler*, 144 F.3d at 670.

Under Oklahoma law, which we apply in this diversity case, *see Wood v. Eli Lilly & Co.*, 38 F.3d 510, 512 (10th Cir. 1994), "[a] plaintiff seeking recovery for an injurious side effect from a properly manufactured prescription drug must prove that the drug caused the injury and that the manufacturer breached a duty to warn of possible detrimental reactions." *McKee v. Moore*, 648 P.2d 21, 23 (Okla. 1982). Causation is established if "in a natural and continuous sequence, unbroken by an independent cause" the drug produces an injury that would not have occurred if it had not been administered. *See Gaines v. Providence Apartments*, 750 P.2d 125, 126-27 (Okla. 1987) (defining proximate cause).

We need not address the Hollanders' argument in detail. We have already ruled that five of the eight categories of evidence on which they rely did not constitute sufficiently reliable grounds under Daubert for their experts' opinions.[18] As a result, these categories of evidence do not raise questions of fact on issues of causation.

Moreover, under Oklahoma law, a plaintiff must introduce expert testimony if "the fact in issue is not within

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18. These categories of evidence are as follows: incidents of dechallenge and rechallenge; case reports; studies of hypertension; the fact that bromocriptine is an ergot; and animal studies.

the realm of ordinary experience of mankind." *Strubhart v. Perry Mem'l Hosp. Trust Auth.*, 903 P.2d 263, 274 (Okla. 1995). Here, the alleged effect of Parlodel is not within the realm of ordinary experience: in order to assess the arguments regarding the alleged effects of the drug, the factfinder would be required to assess the wide variety of scientific evidence that we have discussed here. As a result, the Hollanders cannot prove their claim without expert testimony.

Finally, we consider briefly the three categories of evidence that we have not yet addressed — the FDA determination, the judgment in the *Roberts* case, and the epidemiological studies. None of this evidence provides sufficient support for the Hollanders' claims.

As to the FDA determination, this circuit has noted that differing standards militate against applying regulatory actions to the elements of tort law. *See Mitchell*, 165 F.3d at 783 n.3 (10th Cir. 1999). In assessing a district court's application of *Daubert*, we discounted a state agency's classification of a substance as a carcinogen, stating that the methodology employed by the agency "results from the preventive perspective that the agencies adopt in order to reduce public exposure to harmful substances," and that "[t]he agencies' threshold of proof is reasonably lower than that appropriate in tort law." *Id.* (internal quotation marks omitted).

Moreover, several courts have concluded that this specific FDA ruling about Parlodel is not relevant to the causation question. *See Glastetter*, 252 F.3d at 991 (noting that the FDA ruling is not reliable evidence of causation for

two reasons: (1) because the FDA "balanced Parlodel's possible harm against its limited beneficial use," an irrelevant consideration in the *Daubert* inquiry; and (2) because "[t]he FDA will remove drugs from the marketplace upon a lesser showing of harm to the public than the standards used to assess tort liability"); *Siharath*, 131 F. Supp. 2d at 1366 (rejecting the plaintiff's reliance on the FDA ruling). Moreover, the language used in the FDA ruling regarding the withdrawal of Parlodel indicates that the agency did *not* make a determination that Parlodel causes seizures and strokes.[19] Accordingly, we conclude that the FDA ruling does not establish that there are controverted factual issues as to whether Parlodel caused Ms. Hollanders' stroke.[20]

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19. The FDA ruling states that the evidence received by the FDA "*calls into question* bromocriptine's safety," that bromocriptine "*may* be an additional risk factor in patients who are already at risk for seizures and stroke," and that the FDA had obtained new evidence "*suggesting* that therapeutic use of bromocriptine for the prevention of physiological lactation *may* lead to serious adverse experiences. . . ." 59 Fed. Reg. 43348, 43351 (Aug. 24, 1994) (emphasis added).

20. Our conclusion about the FDA's decision to withdraw the indication for Parlodel as a lactation suppressant should not be read to suggest that, as a general rule, regulatory decisions lack the intellectual rigor necessary under the *Daubert* reliability inquiry. Indeed, some authorities view the review process in the regulatory area as typically "far more careful and systematic" than the peer review process employed by scientific journals. *See* Kenneth R. Foster & Peter W. Huber, *Judging Science: Scientific Knowledge in the Federal Courts* 174 (1997). "Regulators require that documents submitted to them contain far more detail than is typically found in papers submitted to professional journals. . . . [and] administrative reports — not peer reviewed journals — may provide parties with the solidest available data." *Id.* at 174-75.

As to the judgment in the *Roberts* case, the Hollanders fail to explain its relevance. The case was decided under Kentucky law, and our decision is governed by different law and different facts. Moreover, in light of the district court's broad discretion in these matters, the fact that different courts reach difference conclusions as to reliability under *Daubert* does not establish that a legal error has been made by one or the other. *See Brasher*, 160 F. Supp. 2d at 1299 n.17 (noting that inconsistent rulings *Daubert* rulings do not necessarily establish an abuse of discretion).

Finally, the epidemiological studies in question do not support the Hollanders' claim. The district court accurately observed that the Hollanders' own experts did not rely on these studies. Moreover, as the district court further noted, "[a]though several studies have been conducted regarding Parlodel and stroke, none has shown a statistically significant link between them." *Hollander*, 95 F. Supp. 2d at 1236. *See also Siharath*, 131 F. Supp. 2d at 1356-59 (discussing four studies finding no statistically significant association).[21]

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21. The Hollanders also suggest that a totality of the circumstances approach establishes that there are controverted issues of material fact. In essence they maintain that even though each individual category of evidence may be insufficient, all of the evidence considered as a whole raises factual questions as to whether Parlodel caused her stroke. The Hollanders cite no legal authority in support of this approach, and in our view, this argument is inconsistent with *Daubert*. To suggest that those individual categories of evidence deemed unreliable by the district court may be added to form a reliable theory would be to abandon "the level of intellectual rigor" of the expert in the field. *Kumho Tire*, 526 U.S. at 152.

Accordingly, we conclude that the district court properly granted Sandoz's motion for summary judgment.

D. Dismissal of Sandoz, Ltd.

Prior to ruling on the *Daubert* and summary judgment motions, the district court dismissed the Hollanders' claims against the defendant Sandoz, Ltd., a company incorporated in Switzerland with its principal place of business there. Prior to January 1, 1990, Sandoz, Ltd. sold Parlodel in bulk to the defendant Sandoz Corporation. However, after that date, Sandoz, Ltd. became a holding company, conducting no advertising in the United States and owing no manufacturing, distribution, or sales facilities here. In granting Sandoz's motion to dismiss, the district court reasoned that Sandoz, Ltd. "does not have a bank account, a telephone number or any employees, officers or directors in this country; and that it does not actively advertise in the United States." Aplt's App. vol. I, at 344 (Dist. Ct. Order, filed Dec. 10, 1996, at 1). Accordingly, the court concluded that it lacked personal jurisdiction over Sandoz, Ltd., and it dismissed the claims against Sandoz, Ltd. with prejudice.

On appeal, the Hollanders argue that, because Sandoz, Ltd. sold Parlodel to its United States subsidiary (Sandoz) prior to January 1, 1990, Sandoz, Ltd. should be deemed to have continued to do business in the United States through July 1990, when Ms. Hollander suffered her stroke. They contend that it is unlikely that Sandoz, Ltd. would have completely ceased doing business in the United States in the seven month period beginning in January 1990 (when it became a holding company) and July 1990 (when Ms.

Hollander took Parlodel). Additionally, the Hollanders argue that the district court erred in dismissing the claims against Sandoz, Ltd. with prejudice.

The Hollanders' challenge to the court's jurisdictional ruling raises a legal question that we review de novo. *See Wenz v. Memery Crystal*, 55 F.3d 1503, 1505 (10th Cir. 1995). Their argument is undermined by precedent that imposes the burden of proof on the party asserting jurisdiction. *See id.* Because they have offered no evidence to rebut Sandoz, Ltd.'s evidence that it did not do business in the United States after January 1, 1990, we conclude that the district court properly held that it lacked jurisdiction over the company.

However, we further conclude that the district court should not have dismissed the Hollanders' claim against Sandoz, Ltd. with prejudice. Its jurisdictional ruling did not address the merits of the Hollanders' allegations as to Sandoz, Ltd., and, as a result, the claim against Sandoz, Ltd. should have been dismissed without prejudice to filing in an appropriate forum. *See Posner v. Essex Ins. Co., Ltd.*, 178 F.3d 1209, 1221 (11th Cir. 1999) (concluding that the district court erred in dismissing claims against a party with prejudice on jurisdictional grounds and instructing the district court to dismiss the claims without prejudice); *Arrowsmith v. United Press Int'l*, 320 F.2d 219, 221 (2d Cir. 1963) ("A dismissal for lack of jurisdiction . . . does not preclude a subsequent action in an appropriate forum.").

Appendix A

III. CONCLUSION

This case illustrates the continuing importance of the Supreme Court's observation in *Daubert*:

> [T]here are . . . differences between the quest for truth in the courtroom and the quest for truth in the laboratory. Scientific conclusions are subject to perpetual revision. Law, on the other hand, must resolve disputes finally and quickly. The scientific project is advanced by broad and wide-ranging consideration of a multitude of hypotheses, for those that are incorrect will eventually be shown to be so, and that in itself is an advance. Conjectures that are probably wrong are of little use, however, in the project of reaching a quick, final, and binding legal judgment — often of great consequence — about a particular set of events in the past. We recognize that, in practice, a gatekeeping role for the judge, no matter how flexible, inevitably on occasion will prevent the jury from learning of authentic insights and innovations. That, nevertheless, is the balance that is struck by Rules of Evidence designed not for the exhaustive search for cosmic understanding but for the particularized resolution of legal disputes.

Daubert, 509 U.S. at 596-97, 113 S. Ct. 2786. Thus, in Judge Posner's words, "the courtroom is not the place for scientific guesswork, even of the inspired sort. Law lags science; it does not lead it." *Rosen*, 78 F.3d at 319.

Here, the district court characterized the Hollanders' evidence as such guesswork, and that characterization was not unreasonable. The Hollanders' evidence provided support for the FDA's decision to withdraw the indication for Parlodel as a postpartum lactation suppressant, as well as for the decisions of experienced clinicians that the apparent risks of Parlodel outweighed the limited benefits of prescribing the drug as a lactation suppressant. However, the district court did not abuse its discretion in ruling that the Hollanders' evidence did not satisfy the *Daubert* standard of reliability.

Additionally, the district court did not err in denying the Hollanders' motion to remand the case to the Oklahoma state courts or in dismissing the claim against Sandoz, Ltd. However, the court did err in dismissing the claim against Sandoz, Ltd. with prejudice.

Accordingly, we AFFIRM the judgment of the district court in all respects EXCEPT that we REMAND the Hollanders' claim against Sandoz, Ltd. with instructions to dismiss that claim without prejudice.[22]

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22. In light of our conclusion that the federal district court did not abuse its discretion in concluding that Hollanders' expert testimony was unreliable under *Daubert*, as well as our conclusion that the court did not err in granting summary judgment to Sandoz, we need not address the Hollanders' challenge to the dismissal of their products liability claim against Presbyterian Hospital. Even assuming that the dismissal was improper, the Hollanders have failed to explain why the same reliability problems noted by the federal district court do not defeat the Hollanders' products liability claim against Presbyterian Hospital.

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We do note, as Presbyterian Hospital observes in its response brief, that an overwhelming majority of jurisdictions have refused to apply strict liability principles to claims against hospitals and physicians involving the distribution of allegedly dangerous drugs or medical devices. *See, e.g., Royer v. Catholic Med. Ctr.*, 741 A.2d 74 (N.H. 1999) (affirming the dismissal of a products liability claim based on an allegedly defective prosthesis and reasoning that where "a health care provider in the course of rendering health care services supplies a prosthetic device to be implanted into a patient, the health care provider is 'not engaged in the business of selling' prostheses for purposes of strict products liability"); *Cafazzo v. Central Med. Health Servs., Inc.*, 668 A.2d 521, 525 (1995) (rejecting products liability claim based on a prosthesis and reasoning that "hospitals and physicians are not sellers, providers, suppliers, or distributors of products such as to activate 402A" and that the policy reasons for strict liability are not present); *Ayyash v. Henry Ford Health Sys.*, 533 N.W.2d 353, 354 (1995) (rejecting products liability claim against a hospital based on an allegedly defective temporomandibular joint implant and reasoning that when "a putative defendant uses a defective product in the course of providing a service, the courts must decide whether the 'transaction' is primarily a sale or a service" and concluding that "[i]n the case of a physician or hospital rendering medical care courts typically have characterized the 'transaction' as a service" and adopting that characterization for policy reasons); *see generally* Linda A. Sharp, Annotation, *Liability of Hospital or Medical Practitioner under Doctrine of Strict Liability in Tort or Breach of Warranty, for Harm Caused by Drug, Medical Instrument, or Similar Device Used in Treating Patient*, 65 ALR 5th 357, 371 § 2(b) (1999) (noting "the continued reluctance by most courts to apply no-fault products liability principles in actions against medical defendants for injuries caused by medical products"). But *see Thomas v. St. Joseph Hosp.*, 618 S.W.2d 791 (Tex. Civ. App. 1981) (hospital held strictly liable where hospital gown ignited when lighted match

Appendix A

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fell on it); *Silverhart v. Mount Zion Hosp.*, 20 Cal. App. 3d 1022 (Cal. App. 1st Dist. 1971) (hospital would be found liable where not engaged in activities integrally related to primary function of providing medical services — selling a defective product in its gift shop).

Although Oklahoma courts do not appear to have answered this particular question, we have no reason to believe that those courts would disagree with the majority rule and extend products liability to hospitals in circumstances like those in the case at bar. *Cf. Allenberg v. Bentley Hedges Travel Serv., Inc.*, 22 P.3d 223, 230-31 (Okla. 2001) (holding that commercial sellers of used products may not be held strictly liable, "at least if the alleged defect was not created by the seller, and the product is sold in essentially the same condition as when it was acquired for resale"). For that reason, and because the Hollanders did not seek certification in the district court proceedings, we DENY their motion for certification to the Oklahoma Supreme Court. *See Boyd Rosene & Assocs., Inc. v. Kansas Municipal Gas Agency*, 178 F.3d 1363, 1365 (10th Cir. 1999) (observing that "[c]ertification is never compelled, even when there is no state law governing an issue"); *Massengale v. Oklahoma Bd. of Examiners in Optometry*, 30 F.3d 1325, 1331 (10th Cir. 1994) (stating that "[w]e generally will not certify questions to a state supreme court when the requesting party seeks certification only after having received an adverse decision from the district court").

APPENDIX B — ORDER OF THE UNITED STATES DISTRICT COURT FOR THE WESTERN DISTRICT OF OKLAHOMA DATED AND FILED JUNE 12, 1996

IN THE UNITED STATES DISTRICT COURT FOR THE WESTERN DISTRICT OF OKLAHOMA

NO. CIV-96-756-T

DEE HOLLANDER, et al.,

Plaintiffs,

vs.

SANDOZ PHARMACEUTICALS CORPORATION, a New Jersey corporation, et al.,

Defendants.

ORDER

Plaintiffs Dee and Don Hollander instituted this action against defendants Sandoz Pharmaceuticals Corporation, Sandoz Ltd., HCA Health Services of Oklahoma, Inc., d/b/a Presbyterian Hospital ("HAC"), and Presbyterian Health Foundation. Plaintiffs voluntarily dismissed Presbyterian Health Foundation and the state court granted HCA's Okla. Stat. tit. 12, § 2012(B)(6) motion to dismiss on the basis that HCA did not have a duty to warn a patient of the risk of prescription drugs. The remaining defendants then removed the suit on the basis of diversity jurisdiction. The plaintiffs have filed a motion to remand, asserting the state court's

order of dismissal was not final; that removal was improper under § 1446 because the dismissal of HCA was involuntary,[1] and HCA failed to join in the removal.

The motion is denied. The order of dismissal was final;[2] consent of a dismissed defendant to removal is not required; and the fraudulent joinder exception to the involuntary/voluntary rule permits the removal of this action.[3]

Accordingly, the motion to remand is denied.[4]

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1. *The voluntary/involuntary distinction has been applied by the courts even though it is not embodied in the removal statute. E.g.* ***Poulos v. Naas Foods, Inc.****, 959 F.2d 69, 71-71 (7th Cir. 1992).*

2. *The plaintiff has confused Okla. Stat. tit. 12, Ch.2, App. Rule 13(E) with Okla. Stat. tit. 12, § 2012(B)(6).*

3. *"When speaking of jurisdiction, 'fraudulent' is a term of art. 14A Charles A. Wright, et al., Federal Practice and Procedure § 3723 at 354 (2d ed. 1985). Although false allegations of jurisdictional fact may make joinder fraudulent.* ***B., Inc. v. Miller Brewing Co.****, 663 F.2d 545, 549 (5th Cir. 1981), in most cases fraudulent joinder involves a claim against an in-state defendant that simply has no chance of success, whatever the plaintiff's motives."* ***Poulos v. Naas Foods, Inc.,959 F.2d 69, 73 (7th Cir. 1992).***

4. *As noted by the defendants, the plaintiffs do not assert in their motion that HCA was erroneously dismissed from the litigation and, controlling Oklahoma authority supports the state court's dismissal of the hospital.*

Appendix B

IT IS SO ORDERED this 12th day of June, 1996.

s/ [illegible]
UNITED STATES DISTRICT JUDGE

APPENDIX C — ORDER ON MOTION TO DISMISS OF HCA HEALTH SERVICES OF OKLAHOMA D/B/A PRESBYTERIAN HOSPITAL

IN THE DISTRICT COURT IN AND FOR OKLAHOMA COUNTY STATE OF OKLAHOMA

Case No. 95-3342-62

DEE HOLLANDER and DON HOLLANDER,

Plaintiffs,

vs.

SANDOZ PHARMACEUTICALS CORPORATION, a New Jersey corporation, et al.,

Defendants.

ORDER ON MOTION TO DISMISS OF HCA HEALTH SERVICES OF OKLAHOMA D/B/A PRESBYTERIAN HOSPITAL

This matter coming on before the undersigned Judge of the District Court, the Plaintiffs appearing through their attorney of record, James E. Frasier of Frasier & Frasier, the Defendant, Sandoz Pharmaceuticals Corporation, appearing through its counsel of record, Richard M. Eldridge of Rhodes, Hieronymus, Jones, Tucker & Gable, and the Defendant, HCA Health Services of Oklahoma, Inc., d/b/a Presbyterian Hospital, appearing through its counsel of record, Glenn D. Huff and David A. Branscum of Foliart, Huff, Ottaway &

Caldwell, the Court proceeded to hear argument of counsel finds that the Motion to Dismiss be and the same is hereby sustained.

Dated this 10th day of May, 1996.

s/ James B. Blevens
James B. Blevens
JUDGE OF THE DISTRICT COURT

APPROVED

s/ James E. Frasier
James E. Frasier
Attorney for Plaintiffs

s/ Richard M. Eldridge [illegible]
Richard M. Eldridge
Attorney for Sandoz Pharmaceuticals Corporation

s/ Glen D. Huff
Glen D. Huff
David A. Branscum
Attorneys for HCA Health Services of Oklahoma, Inc.

APPENDIX D — ORDER OF THE UNITED STATES COURT OF APPEALS FOR THE TENTH CIRCUIT DATED AND FILED JULY 11, 2002

UNITED STATES COURT OF APPEALS
FOR THE TENTH CIRCUIT

No. 00-6135

DEE HOLLANDER; DON HOLLANDER,

Plaintiff - Appellant,

v.

SANDOZ PHARMACEUTICALS, a New Jersey Corporation; HCA HEALTH SERVICES OF KANSAS, INC., HCA Health Services of Oklahoma, Inc. d/b/a Presbyterian Hospital,

Defendants - Appellees.

ORDER

Filed July 11, 2002

Before **EBEL** and **HENRY**, Circuit Judges, and **ROGERS**, District Judge.*

Appellants' petition for rehearing is denied by the panel that rendered the decision.

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* The Honorable Richard D. Rogers of the United States District Court for the District of Kansas, sitting by designation.

Appendix D

The suggestion for rehearing en banc was transmitted to all of the judges of the court who are in regular service as required by Fed. R. App. P. 35. No member of the panel and no judge in regular active service on the court requested that the court be polled on rehearing en banc so the suggestion for rehearing en banc is also denied.

On the question of whether the district court had jurisdiction at the time of judgment, the appellants argue that this court erred in considering Mr. Hollander's deposition testimony in 1998 to determine his residence at the time of judgement, the only remaining defendant was a corporation with its principal place of business in New Jersey. Whether or not Mr. Hollander resided in Oklahoma or Arkansas, the record establishes that, at the time that the district court entered judgment, complete diversity existed between the plaintiffs and the remaining defendant.

Entered for the Court

PATRICK FISHER, Clerk of Court
by: s/ Opal A. Carter
Deputy Clerk

APPENDIX E — RELEVANT STATUTE

Title 28, United States Code, Section 1441(a)

§ 1441. Actions removable generally

(a) Except as otherwise expressly provided by Act of Congress, any civil action brought in a State court of which the district courts of the United States have original jurisdiction, may be removed by the defendant or the defendants, to the district court of the United States for the district and division embracing the place where such action is pending. For purposes of removal under this chapter, the citizenship of defendants sued under fictitious names shall be disregarded.